UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,888	02/08/2007	Dionisius Elisabeth Florack	294-248 PCT/US	3362

23869 7590 02/12/2009

HOFFMANN & BARON, LLP
6900 JERICHO TURNPIKE
SYOSSET, NY 11791

EXAMINER	
OGUNBIYI, OLUWATOSIN A	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
02/12/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,888	FLORACK ET AL.	
	Examiner	Art Unit	
	OLUWATOSIN OGUNBIYI	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 9-25* is/are pending in the application.

4a) Of the above claim(s) *9,12-17 and 21-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,10,11 and 18-20* is/are rejected.

7)☒ Claim(s) *20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 April 2006* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/15/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-7 and 9-25 are pending in the application.

Claims 1-7, 10-11 and 18-20 are under examination.

Claims 9, 12-17 and 21-25 are withdrawn as being drawn to non-elected invention and/or species.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Drawings

The drawings in this application filed 4/7/06 have been accepted. No further action by Applicant is required.

Information Disclosure Statement

The information disclosure statement filed 6/15/06 has been considered. An initialed copy is enclosed.

Election/Restrictions

Applicant's election with traverse of Group I claims 1-11 and 18-20 with traverse in Paper No. 20081004 is acknowledged. The traversal is as follows:

Arntzen et al do not teach a complex of the invention. Specifically, Arntzen et al. do not teach a complex wherein at least one subunit is unaltered and one or more of the others is fused to a protein of interest. Applicants respectfully point the Examiner to page 5, lines 1-7 of the application where it is clear that the invention is specifically directed to complexes wherein not all subunits are fused to a protein of interest, such as an antigen. Furthermore, the application specifically states that the SEKDEL hexapeptide is not comprised in the definition of a protein of interest according to the invention. In fact, subunits fused to a SEKDEL sequence are regarded as unaltered subunits. See page 6, lines 1-6 of the application. According to the terms of the present application, the complex of Arntzen et al is a complex with six unaltered subunits. Arntzen et al. lack the required at least one subunit fused to a first molecule of interest. Thus, Arntzen et al. do not anticipate the linking concept.

This is not found persuasive because although Applicants point out that the SEKDEL hexapeptide is not comprised in the definition of a protein of interest according to the invention, the groups of inventions listed above still do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The groups of inventions listed above lack unity of invention because even though the inventions of these groups require the technical feature of a protein complex comprising at least two, preferably identical, subunits wherein at least one subunit is unaltered and at least one subunit is fused to a first molecule of interest and wherein the protein complex is able to interact with a cell surface receptor via said subunits, this technical feature is not a special technical feature as it does not make a contribution over the prior art in view of Hirst et al (EP 0372928 A2), 6/13/1990. Hirst et al teaches a fusion protein comprising subunit of **E. coli** heat labile toxin B (LTB) fused to a first molecule of interest (an antigen or epitope from a pathogen responsible for a human or veterinary disease) the fusion protein folds into stable pentamer complexes. Thus, the pentamer complexes comprise 5 identical B subunits (unaltered) and wherein least one of the b subunits is fused (e.g. via a linker) to a first molecule of interest (an antigen or epitope from a pathogen responsible for a human or veterinary disease). See abstract, see p,. 2 lines 16-23, p. 3 lines 30-37 and p. 9 claims 1-14. Said protein complex is able to interact via the subunits with a cell surface receptor (GM1 gangloside). See p. 2 line 21.

Applicants' election of the species enterotoxin of *E. coli* and bacterial antigen as the species of toxin and antigen is also acknowledged.

The requirement is still deemed proper and is therefore made FINAL.

Claims 9, 12-17 and 21-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention and species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 20081004.

Claim Objections

Claim 20 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 20 is drawn to a pharmaceutical composition comprising an effective amount of a vaccine according to claim 19.

Claim 19 is drawn to a vaccine comprising a protein complex according to claim 1 and a pharmaceutically acceptable carrier.

Claim 20 is not further limiting because claim 19 is a pharmaceutical composition i.e. a vaccine and a pharmaceutically acceptable carrier. Since it's a vaccine, it will necessarily comprise an effective amount.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19 and 20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an immunological composition comprising a protein complex according to claim 1 and a pharmaceutically acceptable carrier wherein the molecule of interest is an antigen, does not reasonably provide enablement for a vaccine comprising a protein complex according to claim 1 and a pharmaceutically acceptable carrier. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the nature of the invention, breadth of the claim, the amount of direction or guidance provided and the lack of sufficient working examples.

The claims are drawn to a protein complex comprising at least two, preferably identical, subunits wherein at least one subunit is unaltered and at least one subunit is fused to a first molecule of interest and wherein the protein complex is able to interact with a cell surface receptor via said subunits and compositions or vaccines or pharmaceutical compositions comprising said protein complex.

The specification teaches that the protein complex is to be used as a mucosal vaccine see p. 1 lines 1-2.

The claims are broadly drawn to a protein complex comprising any subunit and any molecule of interest wherein the protein complex interacts with any cell surface receptor. The scope of molecules of interest includes any molecule including that are not antigenic per se, such as reporter molecules such as green fluorescent protein or luciferase, chloramphenical transcetylase, beta-glucorinadase (see p. 19 lines 21- 29).

The specification teachings are limited to protein complexes that comprise subunits of *E. coli* heat labile enterotoxin or cholera toxin of *Vibrio Cholerae* with is able to interact with a cell surface receptor used as a carrier for antigens such as CSFV-E2 homodimer, the trimeric glycoprotein G of viral haemorrhagic septicaemia virus (VHSV-G), trimeric glycoprotein G of Rabies virus (RV G) and vesicular stomatitis virus (VSV G); the homotetrameric phosphoprotein P of Sendai virus (SeV P, canine parvo virus, T cell specific epitope HA (influenza virus hemaglutin eptitope), E2 protein of classic swine fever virus, heat shock protein, cytokines or bacterial antigens etc . See p. 6, see p. 8 lines 8 to 34, p.10-11.

The specification does not correlate the protein complex as set forth in the claims comprising any subunit and any molecule of interest with any protective immune response against any pathogen. In the instant case, the specification has not correlated the production of protective antibodies via immunization with the instant protein complex that comprises any subunit and any molecule of interest with protection against infection from any pathogen. For instance, will a protein complex comprising subunits of *E. coli* heat labile enterotoxin and green fluorescence protein or luciferase induce a protect immune response, and against what pathogen act as a vaccine?

Even, when the molecules of interest are limited to antigens derived from pathogenic microorganisms, vaccines by definition trigger an immunoprotective response in the host vaccinated and mere antigenic response is insufficient. It is well recognized in the vaccine art, that it is unclear whether an antigen(s) derived from a pathogen will elicit protective immunity. Ellis, R.W. (Chapter 29 of "VACCINES" [PIotkin, S.A. et al. (eds) published by W. B. Saunders company (Philadelphia) in 1988, especially page 571, 2nd full paragraph] exemplifies this problem in the recitation that "The key to the problem (of vaccine development) is the identification of that protein component of a virus or microbial pathogen that itself can elicit the production of protective antibodies.... and thus protect the host against attack by the pathogen". In the instant case, the specification has not correlated the production of protective antibodies via immunization with the instant protein complex comprising molecules of interest such as any antigen. The scope of molecules of interest is broad and includes antigen and the scope of antigens is also broad. Even if the molecule of interest are bacterial antigens induction of an immune response does not necessarily translate into protective immunity.

The instant rejection can be overcome by indicating that the molecule of interest is an antigen and replacing vaccine with "immunogenic composition" or “immunological composition” in claims 19-20.

Claims 4 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 is drawn to a protein complex according to claim 1, wherein said complex comprises at least two subunits provided with a molecule of interest.

Claim 5 is drawn to a protein complex according to claim 4, wherein said at least two subunits are provided with a different molecule of interest.

It is not clear in the claims how the subunits are "provided" with a molecule of interest. The recitation of "provided" is vague as it is not clear what structure is conveyed by "provided".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7, 10-11 and 18-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Hirst et al. EP 0372928 A2, 6/13/1990.

The claims are drawn to a protein complex comprising at least two, preferably identical, subunits wherein at least one subunit is unaltered and at least one subunit is fused to a first

molecule of interest and wherein the protein complex is able to interact with a cell surface receptor via said subunits.

Hirst et al teaches a fusion protein comprising a subunit of *E. coli* heat labile toxin B (LTB) fused to a first molecule of interest (an antigen or epitope from a pathogen responsible for a human or veterinary disease) wherein the fusion protein folds into stable pentamer complexes. Thus, the pentamer complexes comprise 5 identical B subunits (unaltered) and wherein least one of the b subunits is fused (e.g. via a linker) to a first molecule of interest (an antigen or epitope from a pathogen responsible for a human or veterinary disease). See abstract, see p,. 2 lines 16-23, p. 3 lines 30-37 and p. 9 claims 1-14. Said protein complex is able to interact via the subunits with a cell surface receptor (GM1 gangloside). See p. 2 line 21.

As to claim 2, said first molecule of interest (antigen or epitope) can associate with a second molecule of interest e.g. covalently bonded to another molecule of interest. See example 1 p. 4 which teaches a recombinant LTB-ST hybrid protein achieved by fusing the gene encoding the B subunit of heat labile enterotoxin to different portions of the gene encoding heat stable enterotoxin – see fig. 1 and p. 4 lines 38-40 for pTHR5 comprising a first molecule of interest i.e. central core region of STa2 associated with a second molecule of interest i.e. carboxy terminal region of the STa2 gene. Claim 2 is drawn to the protein complex and "can associate with, preferably via a covalent bond to a second molecule of interest to form a multimer of interest" is a process limitation. Also, the recitation of 'preferably' does not limit to associate via a covalent bond.

As to claim 3, the protein complex is based on B subunit of heat labile enterotoxin of E. coli.

As to claim 4, said protein complex as set forth above comprises at least two subunits (5 subunits to form the heat labile toxin B) provided with a molecule of interest.

As to claim 5, said protein complex of claim 4 comprising at least two subunits is provided with a different molecule of interest - see example 1 p. 4 which teaches a recombinant LTB-ST hybrid protein achieved by fusing the gene encoding the B subunit of heat labile enterotoxin to different portions of the gene encoding heat stable enterotoxin- thus the protein complex of Hirst comprises at least two subunits provided with a molecule of interest wherein said at least two subunits are provided with a different molecule of interest.

As to claim 6, said GM1 gangloside receptor is present on intestinal epithelial. See instant specification p. 2 lines 13-16.

As to claim 7, Hirst et al teaches that the molecule of interest is a bacterial antigen. See p. 2 lines 48-54.

As to claims 18-20, Hirst et al teaches a composition or vaccine comprising said protein complex and a pharmaceutically acceptable carrier (a pharmaceutical composition comprising effective amounts of the vaccine). See p. 4 lines 18 and 29-34.

Status of the Claims

Claims 1-7, 10-11 and 18-20 are rejected.

Claim 20 is objected to.

Claims 9, 12-17 and 21-25 are withdrawn as being drawn to non-elected invention and/or species.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to OLUWATOSIN OGUNBIYI whose telephone number is 571-272-9939. The examiner can normally be reached on M-F 8:30 am- 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Oluwatosin Ogunbiyi/
Examiner, Art Unit 1645

/Robert B Mondesi/
Supervisory Patent Examiner,
Art Unit 1645